

REMARKS

In the amendments reflected in the claim listing above, claims 22, 27 and 28 have been amended to more particularly point out and distinctly claim the subject matter Applicants regard as their invention. Support for the amendments can be found throughout the specification. Now pending in this application are claims 22-33. No new matter has been added.

The amendments to the claims are being made for the purpose of expediting prosecution and are made without prejudice or waiver. Applicants reserve the right to present the original claims in this or a continuing application.

The Office Action

Applicants note with appreciation the Examiner's consideration of Applicants' previous submissions and the withdrawal of several of the grounds of rejection previously made.

The Examiner appears to maintain the rejection of the claims under 35 U.S.C. 103(a) over a combination of Kuhar (U.S. Patent No. 6,358,492; "Kuhar '492"), Kuhar (US 5,496,953, hereinafter "Kuhar '953"), and Davies (US 6,008,227). This rejection is traversed.

As an initial matter, Applicants note that, in making this rejection, the Examiner appears not to rely on the Clarke patent previously cited. Therefore this reference will not be discussed further herein.

Applicants have discussed the teachings of the Kuhar '492 reference in a previous response. The Kuhar '492 reference discloses certain 3 α tropane analogs in which the ring system is substituted at the 2 position with a methyl ester (a methoxy carbonyl group). In contrast, the pending claims (as amended) are directed to compounds in which the 2 position is substituted with an alkylcarbonyl group. The claimed compounds are not taught nor suggested by the Kuhar '492 reference.

The Kuhar '953 reference discloses tropane analogs in which, as the Examiner has recognized, the bicyclic ring system is substituted at the 3 position with a substituent in the beta orientation (not the alpha orientation as required by the pending claims). In addition, the Kuhar '953 reference does not disclose any compounds in which the bicyclic ring system is substituted at the 2 position with an alkylcarbonyl group, as required by the pending claims. Applicants

therefore contend that the Kuhar '953 reference, alone or in combination with the other references cited by the Examiner, cannot teach or suggest the presently-claimed compounds.

The Davies reference discloses tropane analogs in which, as the Examiner has recognized, the bicyclic ring system is substituted at the 3 position with a substituent in the beta orientation (not the alpha orientation as required by the pending claims). The Davies reference is simply silent concerning tropane compounds substituted at the 3 position with a substituent in the alpha orientation. Applicants therefore contend that the Davies reference, alone or in combination with the other references cited by the Examiner, cannot teach or suggest the presently-claimed compounds.

The Examiner states that:

All three references are directed to 3-aryltropane derivatives having binding affinity for dopamine and serotonin uptake sites . . . Kuhar ['492] provides the motivation to prepare the instant selective dopamine ligands (3-alpha isomers of tropane derivatives) by modifying non-selective dopamine and serotonin ligands (3-beta isomers of tropane derivatives) of Kuhar ['953] and Davies ['227] since Kuhar ['492] teaches the selectivity of 3-alpha isomers for dopamine transporter over 3-beta isomers . . .

Office Action at paragraph 4.

This rejection is traversed. Although the Examiner points to certain teachings of the cited references, there is no teaching or suggestion in any of the references (alone or in combination) that the particular features selected by the Examiner could be, or should be, combined as the Examiner has done. One of ordinary skill in the art would not have a reasonable expectation of success in combining the references as suggested by the Examiner.

As previously noted, while the Examiner has pointed to the Kuhar '492 reference as teaching that the 3-alpha compounds of that reference are more selective for the dopamine transporter than the 3-beta compounds, the Kuhar '492 reference also teaches that the 3-alpha compounds are less potent than the corresponding 3-beta compounds (see, e.g., Kuhar '492 at column 2, lines 1-4). Applicants submit that this actually teaches away from the combination suggested by the Examiner.

It was the discovery of the present inventors that tropane compounds having a 3-alpha substituent, have unexpectedly superior properties when compared to prior art compounds. This

discovery has been described in an article published subsequent to the filing of the present patent application (Meltzer *et al.*, J. Med. Chem. 46(16):3483-3496 (2003)).

Applicants contend that, prior to the present invention and absent the teachings of the present specification, one of ordinary skill in the art would not have been motivated to modify the teachings of the cited references as suggested by the Examiner to arrive at the claimed invention, nor would there have been a reasonable expectation that such modifications would be successful. As the Court of Appeals for the Federal Circuit (CAFC) has stated, an Examiner "cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention." See, e.g., In re Fine, 837 F.2d 1071, 1075, 5 USPQ2d 1780, 1783 (Fed. Cir. 1988).

In the present case, the Examiner has chosen certain isolated features from a variety of references and attempted to combine them to arrive at the claimed invention by using the present disclosure as a blueprint. The Examiner's assertion that this combination would have been obvious appears to be impermissible hind-sight, using the present specification as a blueprint to reconstruct the claimed invention from the isolated teachings of the prior art

Reconsideration and withdrawal of the rejection is proper and the same is requested.

CONCLUSION

It is respectfully submitted that the present application is in condition for allowance. An early consideration and notice of allowance are earnestly solicited.

Applicants believe that additional fees are not required to complete the filing requirements for the subject application or otherwise in connection with this submission. However, if a fee is required, a fee paid is inadequate or credit is owed for any excess fee paid, you are hereby authorized and requested to charge/credit Deposit Account No. 04-1105, under Reference No. 48913CON (70207), Customer No. 21874.

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Respectfully submitted,

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